PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 101253-1 WO	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/GB2004/004474	International filing date *(day/month/year)* 22.10.2004	Priority date *(day/month/year)* 24.10.2003
International Patent Classification (IPC) or national classification and IPC C07D239/91, A61K31/513		
Applicant ASTRAZENECA AB		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☒	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
16.02.2005	13.01.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Zellner, A Telephone No. +49 89 2399-8078

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/004474

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-145 as originally filed

   Claims, Numbers

   1-23 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 17-23

because:

☒ the said international application, or the said claims Nos. 17-23 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	13
	No:	Claims	1-12,14-23
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-23
Industrial applicability (IA)	Yes:	Claims	1-16
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

The following documents (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1= WO00/20402
D2= WO00/5153

The present application relates to 4-oxoquinazolin derivatives and their use as inhibitors of cytokine mediated diseases.

item **V**

1. Novelty (Art. 33(2) PCT)

Document D2 discloses compounds of generel formula (Ia). Their definition partially overlaps with the definition of compounds according to present claim 1 (X = -CONH-, q = 0, Q = (3-7C)cycloalkyl). It is noted that the definition of Q in the abstract of D2 does not correspond to the definition given in the description and in the claims (p. 6, l. 1; p. 10, l. 26; p. 15, l. 3-6; claim 1, p. 123, l. 18). Since the overlap of a generic definition is to be considered novelty-destroying, the subject-matter of present claims 1-12 and 14-23 does not appear to fulfill the requirements of Art. 33(2) PCT.

Individual compounds according to present claim 13 are not disclosed in the cited documents.

2. Inventive step (Art. 33(3) PCT)

Documents D1 and D2 disclose structurally related compounds and their use in the treatment of diseases mediated by cytokines. The presently claimed compounds partly overlap with compounds disclosed in D2 (see novelty). Since D2 relates to the same technical field and it has not been shown that the selection of a particular class of substituents leads to an unexpected result when comparing these compounds with the

structurally closest compounds of D2, the presence of an inventive step cannot be acknowledged. It is noted that p. 51 of the present application discloses data comparing compounds of the application with compounds disclosed in D2, apparently examples 5 and 8 of D2. It is also noted, however, that these compounds do not appear to carry the substituent -X-$(CH_2)_n$-Q bound to the phenyl ring via the carbonyl C-atom, as the compounds presently claimed. It is thus not apparent, which structural difference (i.e. substituent Q or X) is responsible for the improved technical effect. It woudl appear that convincing data should show that a feature which confers novelty (note novelyt objection) is also responsible for a technical effect and that this effect is to be considered surprising or the differing feature not within the routine experimentation of the person skilled in the art. At the present stage, however, the data presently on file do not appear to provide evidence for the presence of an inventive step.

It is noted that the exact nature of the group "Q" and the side chain as such does not appear to be of particular importance for the desired property of the resulting compound since the said group is not limited to a particular class of substituents (D2). It would thus appear that the skilled person will, in order to solve the technical problem of providing further 4-oxoquinazoline derivatives which can be used as inhibitors of cytokine mediated diseases, provide further compounds being closely related to compounds as disclosed in D2. Adding further substituents to a known list would at present not appear to involve an inventive step. In addition, document D1 discloses structurally related compounds having a substituent C_{3-7} cycloalkyl whihc can be attached to the side chain of a phenyl group (general formula (I), substituent R^4, see abstract). The application can thus at present not be considered as to fulfill the requirements of Art. 33(3) PCT.

3. Industrial applicability (Art. 33(4) PCT)

Can be acknowledged for claims 1-16.

item **VII**

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art

disclosed in the document D1 is not mentioned in the description, nor is this document identified therein.

item **VIII**

Substituent R^4 is definded as a (3-6)cycloalkyl group in claim 1. The description, however, refers to a meaning which is not comprised in the said defdinition, i.e. a group "cyclopentenyl". The resulting discrepancy leads to a lack of clarity of the claims (Art. 6 PCT).